REMARKS

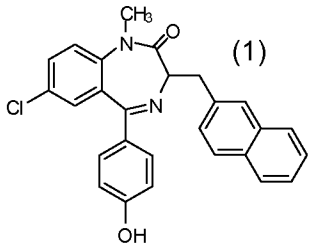
Claims 1 and 13-21 have been amended without any intention of disclaiming equivalents thereof. New claims 22-24 have been added. Claim 12 has been canceled without prejudice to its subsequent reintroduction into this application or its introduction into a related application. Upon entry of this paper, claims 1 and 13-24 will be pending and under consideration. Support for the amendments to claims 1 and 13-21 is provided, for example, in paragraphs 0050, 0051, and 0265-0267 of the published application. Support for new claim 22 is provided, for example, in paragraph 0162 of the published application. Support for new claims 23 and 24 is provided, for example, in paragraphs 0213 and 0236 of the published application, which describe that one embodiment of the invention relates to monotherapy using a single therapeutic agent, e.g., a benzodiazepine described in the application.

In the Office action mailed July 17, 2008, Claims 1 and 12-21 were rejected under 35 U.S.C. §103(a) as being obvious over Kim *et al.*, 1998 Braz. Chem. Vol. 9, No. 4, 375-379 (hereinafter Kim) in view of Punegova *et al.* RU2096044 abstract (hereinafter Punegova) and U.S. Patent No. 6,824,561 to Soykan (hereinafter Soykan). This rejection is addressed below.

Rejection Under 35 U.S.C. § 103(a)

According to pages 2-6 of the outstanding Office action, claims 1 and 12-21 presently stand rejected under 35 U.S.C. § 103(a) as being obvious over Kim in view of Punegova and Soykan. The Office first relies on Kim as teaching compound Bz-423. Office action page 3. The Office then relies on Punegova as teaching a "melatonin based implant composition for controlling biological rhythm in animals" that may optionally include "a psychotropic drug e.g., phenothiazine or benzodiazepine derivatives." *Id.* In order to link the compound described in Kim with the Punegova implant containing a psychotropic drug, the Office action states "the [Kim] reference teaches the recited compound is sharing all the pharmacological activities with benzodiazepine, see page 375." *Id.* Applicant has reproduced below the excerpt from page 375 of Kim describing the pharmacological activity of compound Bz-423.

> In one study, benzodiazepine **1** was identified as the first small molecule inhibitor of autoantibody•DNA interactions in lupus-prone mice[13]. Related autoantibody•DNA interactions have been implicated in the autoimmune disease systemic lupus erythematosus (SLE)[14]. Blocking this interaction could potentially provide the first effective treatment of SLE. In order to perform animal studies to evaluate this potential strategy for treatment, large quantities of benzodiazepine **1** were required.



Applicant submits that, as illustrated by the excerpt above, Kim does not teach that Bz-423 is "sharing all the pharmacological activities with benzodiazepine[s]." Indeed, Kim makes no comparison whatsoever between the biological activity of Bz-423 and the biological activity of other benzodiazepine compounds.

Punegova, as relied upon by the Office, describes a melatonin-based implant for controlling biological rhythm in animals. The purported use for the implant is in "animal breeding and for accelerating the development of fur-bearing animal coats." (Punegova, Abstract) Punegova states that "a psychotropic drug…is optionally included." (*Id.*, emphasis added) The psychotropic drug may be "e.g., phenothiazine or benzodiazepine derivs." *Id.* However, not all benzodiazepine compounds have psychotropic effects. Punegova provides no guidance on selecting particular benzodiazepine compounds, other than the benzodiazepine should have psychotropic effects in the animal. *Id.*

The psychotropic effects of certain benzodiazepines have been linked to binding of the benzodiazepine compound to the central benzodiazepine receptor. See, for example, col. 1 of U.S. Patent No. 6,380,384. One example of a central benzodiazepine receptor modulator is diazepam, which is marketed for treating anxiety. *Id.* In contrast, compound Bz-423 does not bind to the central benzodiazepine receptor. See, for example, paragraphs 0135 and 0189 of the published application. Instead, the instant application describes in, for example, Examples 22-23 that compound Bz-423 binds to mitochondrial F_1F_0-ATPase. It is thought that the anti-proliferative effects of Bz-423 are due to binding of Bz-423 to the mitochondrial F_1F_0-ATPase. See Examples 22-28 of instant application.

In view of the foregoing, Applicant respectfully submits that the subject matter of claim 1, as amended, which is directed to "a drug-eluting stent media coated on a vascular stent" where the stent media comprises the F_1F_0-ATPase inhibitor Bz-423 "in an amount effective to inhibit

restenosis in a subject," would have not been obvious to the skilled artisan based on art applied in the Office action. The teachings of Punegova and Kim provide no reason for the skilled artisan to add compound Bz-423 to the melatonin-based implant of Punegova. As described above, Punegova teaches that the benzodiazepine, if present, is a psychotropic drug. However, Kim makes no indication that Bz-423 has psychotropic properties – moreover Applicant has explained Bz-423 does not bind to the central benzodiazepine receptor. In addition, even if Bz-423 were added to the implant of Punegova, this modification would not achieve the purpose stated in Punegova of optionally adding a psychotropic drug. Soykan does not cure the deficiencies of Punegova and Kim.

In addition to the foregoing, Applicant submits that neither Punegova, Kim, nor Soykan teach or suggest all the limitations of claim 1, as amended. For example, claim 1 requires that Bz-423 is present in the drug eluting stent media in "an amount effective to inhibit restenosis in a subject." Neither Punegova, Kim, nor Soykan teaching using Bz-423 in drug eluting stent media in an amount effective to inhibit restenosis. Beyond this, Applicant submits that neither Punegova nor Kim teach or suggest the feature of claim 1 that the drug-eluting stent media is coated on a vascular stent. The Office has acknowledged that "Kim does not disclose the use of the disclosed compounds in a stent." Office action page 3. Similarly, the Office does not assert that Punegova teaches a stent. Indeed, modifying the melatonin-based implant of Punegova for use in a vascular stent could have undesirable consequences due to the melatonin, which, according to Punegova, is present in concentrations sufficient to artificially alter development of the subject.

Accordingly, Applicant respectfully requests that the rejection of claim 1 be reconsidered and withdrawn. Claims 13-21 depend from and, therefore, incorporate all the limitations of claim 1. In view of the remarks relating to the foregoing independent claims, Applicant respectfully requests that the rejection of dependent claims 13-21 also be reconsidered and withdrawn.

Regarding new claim 22, Applicant submits that neither Kim, Punegova, nor Soykan teach or suggest a drug-eluting stent media that when placed in a subject, the cells in the subject are exposed to Bz-423 at a concentration of less than 10 μM. This concentration of Bz-423 is significant because, as explained in paragraph 0162 of the published application, exposing cells

to Bz-423 at a concentration of less than 10 μM inhibits cellular proliferation, whereas higher concentrations of Bz-423 can lead to apoptosis.

CONCLUSION

Each rejection of the final Office action mailed July 17, 2008 has been addressed. Should the Examiner believe that a telephone interview would aid in the prosecution of this application Applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

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